POINT/COUNTERPOINT

Suggestions for topics suitable for these Point/Counterpoint debates should be addressed to Colin G. Orton, Professor Emeritus, Wayne State University, Detroit: ortonc@comcast.net. Persons participating in Point/Counterpoint discussions are selected for their knowledge and communicative skill. Their positions for or against a proposition may or may not reflect their personal opinions or the positions of their employers.

Simultaneous PET/MR will replace PET/CT as the molecular multimodality imaging platform of choice

Habib Zaidi, Ph.D.
Division of Nuclear Medicine, Geneva University Hospital, CH-1211 Geneva 4, Switzerland
(Tel: 41 22 372 7258; E-mail: habib.zaidi@hcuge.ch)

Osama Mawlawi, Ph.D.
Department of Imaging Physics, The University of Texas M. D. Anderson Cancer Center, Houston, Texas 77030
(Tel: 1 713 563 2711; E-mail: omawlawi@di.mdacc.tmc.edu)

Colin G. Orton, Ph.D., Moderator

(Received 30 March 2007; accepted for publication 30 March 2007; published 17 April 2007)

[DOI: 10.1118/1.2732493]

OVERVIEW

With the combination of PET and CT images in dual-modality PET/CT units, it is now possible to accurately align the functional information obtained with PET to the anatomical structures revealed by CT. This is a significant improvement over previous methods of combining these two modalities by "fusing" images obtained in sequential studies, with all the problems associated with precise patient positioning. The oncological community has so embraced this new technology that PET/CT units are now becoming commonplace. Indeed, PET units are now rarely purchased without being combined with CT. However, many would argue that the anatomical data derived from CT is not as complete as that which could be obtained with MRI, and the metabolic information that can be obtained with PET is somewhat limited compared with that which might be obtained with magnetic resonance, especially with functional MRI (fMRI) and MR spectroscopy (MRS). This has led to the recent development of combined PET/MR units, which are being promoted as even better than PET/CT. The premise that PET/MR will replace PET/CT as the molecular multimodality imaging platform of choice is the topic debated in this month's Point/Counterpoint.

Arguing for the Proposition is Habib Zaidi, Ph.D. Dr. Zaidi received a Ph.D and Habilitation (Privat-docent), both in Medical Physics, from the University of Geneva. He is senior physicist and head of the PET Instrumentation & Neuroimaging Laboratory at Geneva University Hospital, where he is actively involved in the development of imaging solutions for cutting-edge interdisciplinary biomedical research and clinical diagnosis. He is a member of the editorial board and/or serves as scientific reviewer for several scientific journals. He is a senior member of the IEEE and Vice Chair of the Professional Relations Committee of the IOMP. He is involved in the evaluation of research proposals for European and international granting organizations and participates in the organization of international symposia and conferences. He is a recipient of many awards and distinctions and has been an invited speaker of many keynote lectures at an international level.

Arguing against the Proposition is Osama Mawlawi, Ph.D. Dr. Mawlawi received his Ph.D in Biomedical Engineering from Columbia University in NY. He did his graduate training in PET imaging at Memorial Sloan Kettering Cancer Center in New York City before accepting a joint faculty position in the Departments of Radiology and Psychiatry at Columbia University Medical Center, where he focused on neuroreceptor imaging using PET. He is currently an Associate Professor of Imaging Physics at M.D. Anderson Cancer Center in Houston, Texas, and is the lead PET/CT physicist at the center. Dr. Mawlawi is a reviewer for numerous international journals, has been an invited speaker at many national and international conferences, and is the recipient of several grants from public and private sources.

FOR THE PROPOSITION: Habib Zaidi, Ph.D.

Opening statement

The recent introduction of PET/MR technology is considered by many experts to be a major breakthrough that will potentially lead to a paradigm shift in healthcare and revolutionize clinical practice. Several research groups in academic and corporate settings are focusing on the development of various configurations of MR-compatible PET inserts to allow simultaneous scanning using the most highly sophisticated molecular imaging technologies available today.[1–6] Compared to PET/CT, where sequential scanning was (erroneously) considered to be the ultimate solution for image coregistration to correlate structural and functional information thus allowing anatomic localization of abnormal tracer uptake or facilitating the process of differentiating normal from abnormal uptake, simultaneous PET/MR has many additional features. First, for small animal studies, *simultaneous* scanning reduces time under anesthesia and enables scanning under identical physiological conditions. Second, high-field MRI generates high resolution anatomical and structural images offering better soft-tissue contrast resolution and a large variety of tissue contrasts compared to CT, and allows for functional MRI, thus enabling temporal correlation of blood flow with metabolism or receptor expression in brain studies and, more importantly, is capable of assessing flow, diffusion, perfusion, and cardiac motion in one single examination. Third, MRI can be combined with MRS to measure spatially matched regional biochemical content and to assess metabolic status or the presence of neoplasia and other diseases in specific tissue regions. Finally, MRI does not use any ionizing radiation and therefore can be used without restrictions in serial studies, for pediatric cases, and in many other situations where radiation exposure is a concern.

A major advantage cited for PET/CT is that it enables a reduction in the overall scanning time by using CT images for attenuation correction. However, it does this at the expense of a substantial increase in absorbed dose, a significant issue when scanning normal subjects and small animals, as it might change the animal model being studied.[7] In comparison to CT, MRI typically is more expensive, involves longer scan times, and produces anatomical images from which it is more difficult to derive maps for attenuation correction of the PET emission data. However, some solutions do exist as demonstrated by a proof of concept for using segmented MRI-guided attenuation compensation in brain PET,[8] and plenty of opportunities remain for creative advances in MRI-guided attenuation correction in whole-body PET imaging.

Whereas many technical problems have been recently solved, it is recognized that implementation and operation of a combined PET/MR system is still facing many important challenges that must be overcome through research. Many design configurations based on the use of detector readout technologies insensitive to magnetic fields have been proposed, including avalanche photodiodes and, more recently, silicon photomultipliers, particularly for preclinical systems. Moreover, one of the major vendors recently married a PET insert to a 3T MR head scanner,[4] making its application to humans in research settings (and possibly extension to clinical whole-body PET/MR) a near certainty as prototypes are being deployed in some European institutions.

Weighing the advantages and drawbacks of each technology renders the conclusion "*simultaneous PET/MR will replace PET/CT as the molecular multimodality imaging platform of choice*" not only plausible but also obvious. This technology will likely succeed in unifying the four promising molecular imaging techniques PET, structural MRI, fMRI, and MRS, which is in sharp contrast to the limited information provided by dual-modality PET/CT imaging.

AGAINST THE PROPOSITION: Osama Mawlawi, Ph.D.

Opening statement

It is always difficult to predict the extent of success a new technology will achieve particularly when it is still in its infancy as is the case with PET/MR. In general however, for a nascent technology to successfully replace an established standard, its capabilities should not only emulate the standard but also constitute a demonstrable advantage that undeniably leads to its widespread use, while its disadvantages should not offset its potential benefits. In this regard I will argue, for now, that PET/MR will not replace PET/CT as the modality of choice for molecular imaging at least from a *clinical* evaluation standpoint. For research applications on the other hand, much can be said in favor of PET/MR.

PET/MR has the capability of emulating the achievements already established by PET/CT. Scan duration with PET/MR is anticipated to be similar to PET/CT or slightly longer depending on the pulse sequence used.[9] This can, however, only be achieved if the design of PET/MR allows for concurrent rather than sequential data acquisition, as is the case

with PET/CT. Furthermore, the instantaneous fusion of anatomical and functional data, which facilitated the acceptance of PET/CT, can be accomplished with PET/MR[9–11] and the use of MR for attenuation correction, although challenging, is also presumably feasible as has been shown at least for brain imaging.[8] However, as mentioned earlier, for PET/MR to replace PET/CT it should, in addition to emulating the advantages of PET/CT, provide a clinically practical and tangible advantage in image acquisition, interpretation, and diagnosis.

PET/CT is currently mainly used for whole-body oncological evaluations, an application comprising the majority of reimbursable indications for PET/CT.[12] In this regard, for PET/MR to replace PET/CT it should be able to provide a better alternative particularly in whole body imaging. However, since the pairing of MR with PET is not envisioned to further improve the PET imaging portion over what has already been accomplished with CT but rather to augment it with functional (fMRI) or spectroscopic (MRS) data, both of which are not routinely used for diagnostic evaluation, the question then becomes: Is it better from a diagnostic perspective to pair a PET scanner with CT or MR? The answer to this question largely depends on the application, ease of use, and cost. Since its introduction in the early 1980s, MR has steadily gained acceptance, but it has not replaced CT in many areas, mainly because of the reasons above. The same applies to PET/MR replacing PET/CT in routine clinical imaging. Until the diagnostic advantages of whole body PET/MR are well established, reimbursable, and supersede any additional diagnostic advantages that PET/CT might introduce, I believe that PET/MR will be restricted to research and will have difficulty replacing the widely accepted use of PET/CT.

One area where PET/MR has a clear advantage over PET/CT is lower patient radiation exposure. This advantage should by itself be sufficient to predict that PET/MR will replace PET/CT. Unfortunately, however, we have repeatedly seen that efforts for dose reduction are circumvented by other dominating factors such as cost, speed, and ease of use[13,14] suggesting that this reasoning might not be strong enough to induce the suggested change in PET imaging.

In summary, PET/MR scanners have a lot of potential advantages. However, for these advantages to assist PET/MR in replacing PET/CT in routine clinical evaluation, they first have to be cost effective and easy to realize and, most importantly, become a necessary component of the routine whole body diagnostic evaluation of cancer patients using PET imaging.

Rebuttal: Habib Zaidi, Ph.D.

I concur with my colleague that current PET/CT technology is more comfortable for end-users and that the use of PET/MR in clinical and research settings requires extensive technical and organizational efforts that may restrict its use in the short term to academic centers having the required scientific resources. I also agree that any new technology should be assessed carefully with respect to benefits conveyed to patients before widespread acceptance and adoption. We clearly need large-scale studies to demonstrate the clinical benefits of PET/MR and, more importantly, to define where PET/CT is sufficient and where PET/MR is needed. However, I disagree with the main arguments raised to claim that PET/CT is, and will remain, the clinical standard in the foreseeable future. First, combined PET/MR is also aiming at improving the diagnostic relevance of the PET imaging portion but in a more profound way, which is not limited to providing anatomical information for mapping of metabolic abnormalities and shortening transmission scanning time, as PET/CT does. In addition to offering a diversity of tissue contrasts, MR will provide a wealth of additional information through fMRI and MRS to enhance the diagnostic performance and quantitative capabilities of PET. More importantly, using simultaneous (rather than sequential) scanning will resolve many of the impediments to precise coregistration of anatomo-molecular information and accurate attenuation correction. Second, reimbursement issues are mainly driven by prospective clinical studies that demonstrate improvements in health outcomes conveyed by an imaging modality for a given indication. Therefore, given the higher soft tissue contrast resolution of MRI and its highest sensitivity and specificity for many indications (e.g., detection of liver metastases),[9] coverage for PET scans will undoubtedly be expanded.

This having been said, I would like to challenge my colleague further by asking: "Is PET/CT unanimously recognized as the standard imaging technology for clinical oncology?" One should bear in mind that this is still a controversial issue, since many investigators claim that it has a limited role in many indications including lymphomas, lung nodules, and brain tumors.[15] Time will dictate whether PET/MR will influence the standard for future PET instrumentation, which is poised to advance molecular imaging and influence clinical and research practice.

Rebuttal: Osama Mawlawi, Ph.D.

I agree with Dr. Zaidi that PET/MR has many potential advantages, provided that current technological barriers facing its development are resolved. As I mentioned in my opening statement, PET/MR theoretically provides the same advantages that PET/CT provided to dedicated whole body PET imaging such as anatomical landmarks, shorter scan durations, and attenuation correction. In addition, PET/MR potentially can augment PET imaging with a wealth of other information such as functional and spectroscopic data that may be helpful in improving patient management as well as understanding tumor biology. Furthermore, with PET/MR this information is obtained at a reduced patient radiation exposure compared to PET/CT. So in essence, pairing PET with MR can only provide an added advantage over PET/CT. However, going as far as suggesting that PET/MR will replace PET/CT might be premature at this stage, particularly since none of the suggested added advantages of PET/MR

have been shown to be clinically justified, practical and, most importantly, cost effective in routine whole body oncological imaging.

There is no doubt that in order to assess the need for PET/MR in a clinical setting, such a hybrid modality should be made available at least in large research centers. Results from studies conducted on these systems will then provide the necessary data to justify their routine clinical use and eventually convince the medical community about the merits and cost effectiveness of PET/MR. Until that happens, I believe that PET/CT will continue to be the modality of choice in whole body oncological imaging.

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